REMARKS

Formal Matters

Claims 1- 36 are pending in the application. Claims 5-8, 15-20, 25 and 26 are currently withdrawn from consideration.

Claims 1-4, 9-14, 21-23, 27 and 29 are rejected.

Claim 24 was allowed. Claim 28 was objected to.

The drawings are amended herein as proposed in the previous response so as to recite sequence identifiers.

The Office Action of April 22, 2003 does not indicate whether the office entered the amendments to the Specification to make the figure numbers reflect those of the formal (replacement) drawings. If not previously entered, Applicants request entry of these amendments.

The specification is amended to replace the Sequence Listing, which in turn is amended to include the sequence MEWRNKKRSDWLSMVLRTAGVE as SEQ ID NO:21. Support for this amendment is found in the specification at, for example, page 8, lines 12-15; Fig. 1 (particularly panel C, now referred to as Fig. 1C), page 9, lines 19-20 and Fig. 5; page 9, lines 25-26 and Fig. 6; and page 16, lines 11-13.

Claims 1-4, 13, 14, 21-23, and 26-27 are amended. Support for these amendments is found in the specification at, for example: page 2, lines 24-30; page 3, lines 5-17; page 4, line 20 to page 5, line 2; page 6, lines 16-34, page 8, lines 12-15; Fig. 1 (particularly panel C, now referred to as Fig. 1C), page 9, lines 19-20 and Fig. 5; page 9, lines 25-26 and Fig. 6; and page 16, lines 11-13 (claims 1-4, 13, 14, 21-23, and 27); claims 1 and 26 as originally filed and previously presented, respectively (claim 26).

New claims 30-36 are added, which claims find support in, for example, original claims 9-14.

The amendments presented herein introduce no new matter, and further raise no new issues which require, for example, a further search. Entry of these amendment is respectfully requested.

Claims Withdrawn

Claims 5-9, 15-20 and 25-26, as well as claim 1-5, 9-14 and 21-24 in so far as they are drawn to complementary nucleic acids are currently withdrawn. Applicants have filed a Petition for Reconsideration of the Restriction Requirement with respect to nucleic acids and their complements being restricted into separate groups.

Applicants thank the Examiner for noting the claim 26 can not properly depend from claim 1. Applicants have attended to this by amendment of claim 26.

Statement Regarding the Sequence Listing

I hereby certify that the enclosed Sequence Listing is being submitted under 37 CFR §§ 1.821(c) and (e) in paper and computer readable form (Compact Disk labeled 'CRF').

As required by 37 CFR 1.821(f), I hereby state that the content of the paper and computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. §1.821(c) and (e) are the same. The Computer Readable Format (CRF), being submitted under 37 CFR §§ 1.52(e) and 1.824, is formatted on IBM-PC, the operating system compatibility is MS-Windows and the file listing is:

Seqlist.txt 32 KB created July 8, 2003.

I hereby certify that the enclosed submission includes no new matter. The Sequence Listing was prepared with the software FASTSEQ, and conforms to the Patent Office guidelines. Applicant respectfully submits that the subject application is in adherence to 37 CFR §§ 1.821-1.825.

Drawing Correction

The Examiner is respectfully requested to enter the proposed amendments to the drawings by replacing the drawings with their corresponding amended drawings submitted herewith. The drawings are amended to include the sequence identifiers.

Claims Objection

Claim 28, which was indicated to be otherwise allowable, was objected to for failing to recite a sequence identifier in the claim. Claim 28 is amended to recite a sequence identifier as requested in the Office Action.

Applicants respectfully submit that this claim is now in form for allowance.

Allowable Subject Matter

Applicants thank the Examiner for indicating that claim 24 is allowable as written (Office Action page 2, item 6) and that claim 28 is objected to but otherwise allowable once the objection is addressed (Office Action page 3, item 7). Claim 28 is amended to recite a sequence identifier, and thus claims 24 and 28 are in form for allowance.

Rejection Under §112, ¶1 – Written Description

Claims 1-4 and 9-14 were rejected on the grounds that the specification does not provide an adequate written description. This rejection is respectfully traversed as applied and as it may be applied to the pending claims.

As applicants understand it, the written description rejection appears to be grounded in 1) the recitation of "fragment" in the claims; and 2) the recitation of a percent sequence identity in the claims.

With respect to recitation of sequence identity in the claim, applicants respectfully submit that the standard to which applicants are being held is not commensurate with the requirements of 35 U.S.C. §112, ¶1. The standard for written description has been established over several

years of court cases such as *Vas-Cath Inc. v. Mahurkar*[1] and *In re Wertheim*[2] and has culminated in the publication of the "Written Description Guidelines" Federal Register Vol. 66 No. 4, dated January 5, 2001 to which the Office must adhere to when making a written description determination. The law of written description does not require that the specification specifically describe all species that are encompassed by the claims.

A landmark and oft-cited case involving written description of nucleic acid invention is *Regents of the University of California v. Eli Lilly & Co*[3], which states that:

> "A description of a genus of cDNAs may be achieved by means of a recitation of **a representative number of cDNAs**, defined by nucleotide sequence, falling within the scope of the genus **or** of a recitation of **structural features** common to the members of the genus."

As such, according to the law, the written description requirement for a genus of nucleic acids may be satisfied by a) a representative number of species, **or** b) a recitation of structural features common to all members of the species.

The result of the application of the law to other similarly postured applications has resulted in the issuance of claims directed to a polynucleotide having a sequence having a recited percent sequence identity (actually "homology" which is even broader), where the encoded protein had a certain activity. For example, see US Pat. No. 6,472,516, with claim 1 being exemplary:

> 1. An isolated DNA molecule comprising a nucleotide sequence more than 80% homologous to any one of the nucleotide sequences shown at:
>
> (i) FIG. 2B (SEQ ID NO:1) from nucleotide 1 to 3018, and
>
> (ii) FIG. 2B (SEQ ID NO:1) from nucleotide 141 to 3018, wherein said DNA molecule encodes a protein with phosphofructo-2-kinase/fructose-2, 6-biphosphatase activity.

In the instant claims, the polynucleotides are claimed as encoding exon 1d of the human VDR (hVDR) gene, and thus are defined by this common structural feature. Exon 1d, as well as

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1 *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991).
2 *In re Wertheim* 191 U.S.P.Q. 90 (C.C.P.A. 1996)
3 *Regents of the University of California v. Eli Lilly & Co* 119 F.3d 1559 (Fed. Cir. 1997) at 1568-69

an example of a nucleotide sequence encoding exon 1d, is provided (see, e.g., Fig. 4). Several examples of polynucleotides encoding a hVDR isoform having exon 1d are also provided (see, e.g., Fig. 1C, original Fig. 5 (transcript 6), original Fig. 6 (transcript 9), and original Fig. 7 (transcript 10)). Applicants respectfully submit that the amended claims are well within the bounds of the law of written description.

As to fragments, applicants note that the Office Action asserts that a "fragment of a nucleotide can consist of as little as a single base." This is simply not the case – as the fragment must still encode a hVDR isoform (e.g., claim 1) and, more specifically, encode exon 1d of a hVDR. Thus, claim 1 did not – and does not – encompass "any isolated polynucleotide encoding a human vitamin D receptor isoform, irrespective of the sequence of that polynucleotide". Nevertheless, applicants respectfully submit that the amended claims obviate this rejection.

In view of the above, withdrawal of all rejection of the claims under §112, ¶1 is respectfully requested.

Rejection Under §112, ¶1 – Enablement

Claims 1-4 and 9-14, and claims 21-23, 27 and 29, were rejected on the grounds that the specification does not provide an enabling disclosure. This rejection is respectfully traversed as applied and as it may be applied to the pending claims.

The Office Action has taken the position that the specification does not provide guidance needed to "alter any one of those four amino acid sequence [sic] disclosed therein at even a single residue with a reasonable expectation that the resulting protein will function as a vitamin D receptor." This is not a reasonable assessment of the level of skill in the art in 1997, the year in which the instant application was first filed. The ordinarily skilled artisan, given the instant specification and the knowledge in the hVDR art, would understand that, for example, one can readily introduce conservative amino acid changes into the hVDR and reasonably expect to retain function. Furthermore, activity of the hVDR, and assays for assessing its function, are known in the art.

Further arguments were detailed in the prior response, and are not reiterated here.

In the context of the rejection of claims 21-23, 27 and 29, the Office Action states that applicants arguments against the rejection were based on the premise that the degeneracy of the genetic code would allow one to alter the referenced nucleotide sequence without affecting its function. The Office stated that such "arguments would be persuasive if the claims were directed to an isolated polynucleotide which was defined solely by an amino acid sequence encoded thereby." (Office Action, page 6).

Without conceding as to the grounds for this rejection, applicants have amended claims 1-4, and 9-14 to recite that the claimed polynucleotide shares a recited percent sequence identity with a polynucleotide encoding exon 1d of a human VDR (claims 1-4 and 9-14). Claims 21-23, 27 and 29 are amended to recite that the claimed polynucleotide shares a recited percent sequence identity the amino acid sequence MEWRNKKRSDWLSMVLRTAGVE.

Withdrawal of the rejection under §112, ¶1 as applied to claims 1-4, 9-14, and 21-23, 27 and 29 is respectfully requested.

Rejection under §112, ¶2

Claim 3 was rejected as being indefinite for "the repeated occurrence of the term 'of, of'". This rejection is obviated by amendment, and can be withdrawn.

Rejection Under §102(a)

Claims 1, 2, 10, 13 and 14 were rejected as being anticipated by MacDonald et al. (*J. Biol. Chem.*, 266:18808-18813 1991). This rejection is traversed as applied and as it may be applied to the pending claims.

The grounds for rejection appears to be based on the asserted interpretation of "fragment", which the Office has taken to mean as little as a single nucleotide of a recited sequence. Again, applicants take exception to this interpretation of the term, as set out above.

Nevertheless, and without conceding as to the grounds for rejection, applicants respectfully submit that this rejection no longer applies to the claims as currently pending, and can be withdrawn.

CONCLUSION

Applicants respectfully submit that all of the claims in the present application are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please contact either attorney listed below at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RICE-014.

Respectfully submitted,
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Date: July 15, 2003

By: _____
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Enclosures:

Amended Replacement Drawings with Transmittal for Submission of Formal Drawings.

Sequence Listing (hard copy and CRF on CD-ROM)